

### REMARKS

A check for the fee for a two month extension of time accompanies this response. Any fees that may be due in connection with the filing of this paper or with this application may be charged to Deposit Account No. 06-1050. If a Petition for Extension of time is needed, this paper is to be considered such Petition.

Claims 1-16, 30 and 34 are pending in the instant application. Claim 33 is cancelled. Claim 34 is added. Basis for added claim 34 can be found, for example, at page 7, lines 1-7, page 33, lines 21-30 and in original claim 18. In the interests of advancing the application to allowance, claims 1, 5 and 9 are amended herein. Application reserves the right to file a continuation application to any of the cancelled subject matter.

Since the instant Office Action indicated that claim 33 contained allowable subject matter if rewritten in independent form, the limitations of claim 33 are incorporated into claim 1 as amended herein. As amended, claim 1 incorporates the limitation that the large nucleic acid molecules are labeled with a nucleotide analog, nucleoside analog or a ribonucleoside analog. The amendment to claim 1 recites particular metabolic labels, thus incorporating the limitation of claim 33 that the cells are metabolically labeled. Claim 1 also is amended to remove the reference to "intact and condensed," which is extraneous. Basis for these amendments can be found, for example, at page 7, lines 1-7 and in original claim 1. Thus, claim 1 and all claims dependent thereon should be allowable. Since claims 5 and 9 also were deemed allowable if rewritten in independent form, claims 5 and 9 are rewritten herein as independent claims, incorporating all of the limitations of the previous claim 1. Hence, all pending claims should be allowable.

#### **Rejection of claims 1-4 and 11-15 under 35 U.S.C. §103(a)**

The instant Office Action maintains the rejection of claims 1-4 and 11-15 under 35 U.S.C. §103(a) as being obvious over either Felgner *et al.* or Zelphati *et al.* in view of Nolan *et al.* The Office Action alleges that it would have been obvious to one of ordinary skill in the art to have modified the methods of delivering, detecting and expressing labeled nucleic acid molecules allegedly taught by Felgner *et al.* or Zelphati *et al.*, with the methods of delivering fluorescently labeled chromosomes into cells allegedly taught by Nolan *et al.*, to arrive at the instantly claimed subject matter.

Applicant respectfully maintains that these references, singly or in combination, do not teach or suggest a method for detecting or determining delivery and expression of a nucleic acid introduced into a cell that includes introducing labelled large nucleic acid molecules that encode a reporter gene into cells, detecting labelled cells as an indication of delivery of the nucleic acid into a cell; and measuring the product of the reporter gene as an indication of DNA expression in the cell, whereby delivery and expression of nucleic acid molecules in the cell is detected or determined.

Nonetheless, in the interest of advancing the application to allowance, claim 1 and claims dependent thereon are amended herein to incorporate the limitation that the labelled large nucleic acid is labelled with a nucleotide analog, a nucleoside analog or a ribonucleoside analog. This limitation, incorporated from claim 33, was deemed allowable by the Examiner in the instant Office Action. As the Examiner has acknowledged, none of the references, singly or in combination, teaches or suggests a method for detecting or determining delivery and expression of a nucleic acid introduced into a cell that includes introducing labelled large nucleic acid molecules that encode a reporter gene into cells, where the large nucleic acid molecules are labeled with a nucleotide analog, nucleoside analog or a ribonucleoside analog, detecting labelled cells as an indication of delivery of the nucleic acid into a cell; and measuring the product of the reporter gene as an indication of DNA expression in the cell, whereby delivery and expression of nucleic acid molecules in the cell is detected or determined. Therefore, the rejection of claims 1-4 and 11-15 over Felgner *et al.* or Zelfhati *et al.* in view of Nolan *et al.* is rendered moot. Applicant respectfully requests reconsideration and withdrawal of the rejection.

**Rejection of claims 1, 6-8, 14, 16, and 30 under 35 U.S.C. §103(a)**

Claims 1, 6-8, 14, 16, and 30 are rejected under 35 U.S.C. §103(a) as unpatentable over Felgner *et al.* in view of Nolan *et al.* and in view of Giese *et al.* With respect to claims 1 and 6-8, the Office Action alleges that Felgner *et al.* specifically teaches the use of GFP for detecting or determining delivery and expression of a nucleic acid. Further, it is alleged that Giese *et al.* teaches other reporter genes conventional at the time of filing. With respect to claims 14, 16 and 30, the Office Action alleges that Nolan *et al.* teaches generation of transgenic animals, and therefore one of ordinary skill in the art would know that embryonic stem cells would be used for introduction of nucleic acid. The Office Action concludes that

one of ordinary skill in the art could combine the teachings of Felgner *et al.*, in view of Nolan *et al.* and Giese *et al.* to arrive at the instantly claimed subject matter.

Applicant submits that these references, singly or in combination, do not teach or suggest the claimed subject matter. The combination of references does not teach a method for detecting or determining delivery and expression of a nucleic acid introduced into a cell that includes introducing labelled large nucleic acid molecules that encode a reporter gene into cells, detecting labelled cells as an indication of delivery of the nucleic acid into a cell; and measuring the product of the reporter gene as an indication of DNA expression in the cell, whereby delivery and expression of nucleic acid molecules in the cell is detected or determined. Further, the combination of references does not teach such methods with particular reporter genes as set forth in the instant claims. The combination of references also fails to teach such methods in embryonic cells or any other cell types as instantly claimed.

Nonetheless, in the interests of advancing the application to allowance, claim 1 and claims dependent thereon are amended herein to incorporate the limitation that the labelled large nucleic acid is labelled with a nucleotide analog, a nucleoside analog or a ribonucleoside analog. This limitation, incorporated from claim 33, was deemed allowable by the Examiner in the instant Office Action. As the Examiner has acknowledged, none of the references, singly or in combination, teach or suggest a method for detecting or determining delivery and expression of a nucleic acid introduced into a cell that includes introducing labelled large nucleic acid molecules that encode a reporter gene into cells, where the large nucleic acid molecules are labeled with a nucleotide analog, nucleoside analog or a ribonucleoside analog, detecting labelled cells as an indication of delivery of the nucleic acid into a cell; and measuring the product of the reporter gene as an indication of DNA expression in the cell, whereby delivery and expression of nucleic acid molecules in the cell is detected or determined. Moreover, the references do not teach or suggest such a method with particular reporter genes or in specified cell types as set forth in the instant claims. Therefore, the rejection of claims 1, 6-8, 14, 16, and 30 over Felgner *et al.* in view of Nolan *et al.* and in view of Giese *et al.* is rendered moot. Applicant respectfully requests reconsideration and withdrawal of the rejection.

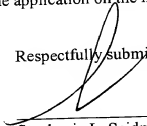
Applicant : De Jong et al.  
Serial No. : 09/815,981  
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AMENDMENT AND RESPONSE

Attorney's Docket No.: 17084-018002  
(24601-416B)

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In view of the above, examination of the application on the merits and allowance is respectfully requested.

Respectfully submitted,

  
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Attorney Docket No. 17084-018002 (17084-416B)

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